Alovudine

Drug Class: **Nucleoside Reverse Transcriptase Inhibitors**

Drug Description

Alovudine, also known as MIV-310, is a synthesized 2',3'-dideoxypyrimidine nucleoside reverse transcriptase inhibitor (NRTI). [1] Alovudine is structurally similar to zidovudine, differing only at the 2' and 3' positions of the ribose moiety. Zidovudine is characterized by an azido group at the 3' position; alovudine has a fluoro group at this position. [2]

HIV/AIDS-Related Uses

Alovudine has been investigated in Phase II trials for the treatment of HIV-1 and -2. Early trials were halted because of unacceptable hematologic toxicity and a lack of benefit compared with zidovudine.[3] Active investigation was resumed, and alovudine entered Phase II trials in HIV infected patients failing multiple antiretroviral therapy.[4] However, in a phase II trial completed in 2005, low-dose alovudine did not achieve the target level of efficacy; the manufacturers subsequently decided to halt development and focus research on more plausible targets.[5]

Pharmacology

Alovudine inhibits HIV replication by mimicking thymidine. When alovudine is incorporated into the DNA strand during synthesis, premature chain termination occurs.[6]

In a concentration-controlled trial involving 14 HIV infected patients, unacceptable hematologic toxicity occurred when the area under the concentration-time (AUC) curve during a 12-hour dosing interval was at least 300 ng-hr/ml. In this trial, alovudine resulted in concentration-dependent reductions of p24 antigen and peripheral blood mononuclear cell HIV titers within 4 weeks of treatment initiation.[7]

Alovudine has potent activity in vitro against multidrug-resistant HIV strains. Multidrug-resistant isolates exhibiting fivefold to 100-fold increases in zidovudine resistance achieved alovudine inhibitory concentration (IC) 50 values of 0.0014 to 0.0162 microM, which are lower than or similar to values for wild type virus. In this study, cellular toxicities of alovudine and zidovudine fell into a similar range, and development of alovudine-resistant isolates was slower than in other NRTIs.[8]

A Phase II trial in patients with multidrug-resistant HIV evaluated alovudine 2 mg for 4 weeks. Alovudine displayed activity comparable to approved antiviral therapies and no serous adverse events. However, the drug did not achieve the target level of efficacy that had been previously defined. The manufacturers chose to halt further study in favor of other existing antiretroviral medication research.[9]

Adverse Events/Toxicity

Early studies of alovudine 20 mg daily showed unacceptable hematologic toxicity, specifically severe anemia and neutropenia.[10] More recent studies of alovudine 7.5 mg and 2 mg daily showed no serious adverse events.[11] [12]

Clinical Trials

For information on clinical trials that involve Alovudine, visit the ClinicalTrials.gov web site at http://www.clinicaltrials.gov. In the Search box, enter: Alovudine AND HIV Infections.

Dosing Information

Mode of Delivery: Oral.[13]

Dosage Form: Liquid.[14]

Chemistry

CAS Name: Thymidine, 3'-deoxy-3'-fluoro-[15]

CAS Number: 25526-93-6[16]

Molecular formula: C10-H13-F-N2-04[17]

Molecular weight: 244.22[18]

Alovudine

Other Names

MIV-310[19]

Further Reading

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Manufacturer Information

Alovudine
Medivir UK Ltd
Chesterford Research Park
Little Chesterford, Essex, United Kingdom
44(0)-1-799-532-100

For More Information

Contact your doctor or an AIDSinfo Health Information Specialist:

• Via Phone: 1-800-448-0440 Monday - Friday, 12:00 p.m. (Noon) - 5:00 p.m. ET

• Via Live Help: http://aidsinfo.nih.gov/live_help Monday - Friday, 12:00 p.m. (Noon) - 4:00 p.m. ET

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